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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,815	04/30/2001	Gary E. Rehm	MSE #2610	3326

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[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1641  
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14

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/844,815	REHM ET AL.
	Examiner	Art Unit
	Gary W. Counts	1641

-- The MAILING DATE of this communication appears in the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 27 November 2002.
  - 2a) This action is FINAL.                    2b) This action is non-final.
  - 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.
- Disposition of Claims**
- 4) Claim(s) 1-14 is/are pending in the application.
  - 4a) Of the above claim(s) 11-14 is/are withdrawn from consideration.
  - 5) Claim(s) \_\_\_\_\_ is/are allowed.
  - 6) Claim(s) 1-10 is/are rejected.
  - 7) Claim(s) \_\_\_\_\_ is/are objected to.
  - 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All
  - b) Some \*
  - c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
  - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)           | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ .                                   |

## **DETAILED ACTION**

### **Status of the claims**

The RCE and corresponding amendment filed on November 27, 2002 is acknowledged and has been entered.

#### ***Priority***

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

#### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. On page 10, lines 14-19 in the specification. Applicant discloses "Phosphate and carboxyl groups are common as the charged ionizable groups of buffering agents and calcium salts of these groups are not very water soluble (calcium phosphate is relatively insoluble), so they tend to precipitate from solution." The applicant does not disclose that the calcium present in the buffered assay medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with the polycarboxylic

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chelating agent. There is no description in the specification disclosing that the buffered assay medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with the polycarboxylic chelating agent.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 7 "in sufficient quantity" is vague and indefinite. It is unclear what is considered to be a sufficient quantity because there is no definition or guidance provided for the phrase in the specification.

#### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-4 and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uenoyama et al (US 5,856,117) in view of Berry et al (US 5,384,247).

Uenoyama et al disclose a method for measuring the concentration of urinary trypsin inhibitors which involves mixing a urine sample, trypsin, and a buffer solution and the addition of a substrate solution to cause the enzyme reaction, and measuring the activity of trypsin (col 5, lines 39-60). Uenoyama et al also teach the use of

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dimethylformamide as the solvent (col 6, line 11) and a buffered pH of 7.8 (col 7, line 46) and the substrate present in a concentration of 1 to 50 mmol/l (col 4, line 16) and trypsin in the concentration of 10 to 500 mg/l preferably 20 to 100 mg/l (col 5, line 52).

The method of Uenoyama et al differs from the instant invention in failing to disclose the use of a polycarboxylic chelating agent to inhibit interference of calcium present in the urine.

Berry et al (US Patent 5,384,247) teach the use of EGTA and EDTA as chelating agents which inhibit the interfering ions of calcium in a urine sample (col 4, line 53 - col 6, line 17) (claims 27 and 34). The use of these chelating agents reduce the free concentration of interfering ions to levels where interference is no longer significant and increase the sensitivity of the enzyme to an analyte with respect to the interfering ion (col 3, lines 45-52).

It would have been obvious to one of ordinary skill in the art to incorporate the polycarboxylic chelating agents of Berry et al into the method of Uenoyama et al because Berry et al shows that the use of these chelating agents provide the advantage of reducing the free concentration of interfering ions to levels where interference is no longer significant and also increase the sensitivity of the enzyme to an analyte.

With respect to the specific concentration of the chelating agents recited in the instant claims, the optimum concentration of chelating agent can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art.

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7. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uenoyama et al in view of Berry et al as applied to claims 1-4 and 7-9 above, and further in view of May et al (GB 2,204,398 A).

See above for teachings of Uenoyama et al and Berry et al.

Uenoyama et al and Berry et al differ from the instant invention failing to disclose dry test reagents and a dry test device which the urine test sample can flow by dipping the dry test device into the buffered assay medium.

May et al disclose a device comprising a hollow casing constructed of moisture-impervious solid material containing a dry porous carrier which communicates indirectly with the exterior of the casing, a sample receiving member protrudes from the casing such that a liquid test sample can be applied to the receiving member and permeate to the porous carrier which contains impregnated reagents ( page 15, lines 16-35 and page 16, lines 1-9). This diagnostic test device allows for quick and convenient use and requires the user to perform as few actions as possible (page 2, lines 29-35).

It would have been obvious to one of ordinary skill in the art to use the device of May et al to practice the method of Uenoyama et al as modified by Berry et al, because May et al shows that the device allows for quick and convenient use and requires the user to perform as few actions as possible, where all the necessary reagents are all present on a single solid support.

8. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ueoyama et al in view of Berry et al as applied to claims 1-4 and 7-9 above, and further in view of Nanbu et al (US 6,130,055).

See above fro teachings of Uenoyama et al and Berry et al.

Uenoyama et al differ from the instant invention in failing to disclose arginine or lysine derivatives as the substrate for trypsin.

Nanbu et al discloses a method for measuring the concentration or activity of urinary trypsin inhibitor. Nanbu et al teach mixing a sample, trypsin solution, and a substrate in a solution and measuring the trypsin activity. Nanbu et al also teach that this substrate may come from the amino acid residues of the L-type (col 2, lines 13-23). The use of this substrate would allow for excellent solubility.

It would have been obvious to one of ordinary skill in the art to incorporate the trypsin substrates of Nanbu et al into the method of Uenoyama et al as modified by Berry et al because Nanbu et al shows that the use of the L-type amino acid residues allows for excellent solubility (col 2, line 23).

### ***Response to Arguments***

9. Applicant's arguments filed November 27, 2002 have been fully considered but they are not persuasive.

Applicant argues that the transitional phrase "consisting essentially of" limits the scope of the claimed invention because claim 1 now recites that the "calcium ions present in the buffered assay medium are not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with the polycarboxylic chelating agent". This is not found persuasive because it is unclear what is considered to be in sufficient quantity and the claim as recited incorporates an amount of calcium

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still present in the instant claims. Therefore, it is the Examiner's position that the claims still read on Uenoyamas reference because the claims as recited contain calcium.

Applicant further argues that the addition of additional calcium is not necessary and is even detrimental since in the method of Uenoyma et al., the calcium interference is not removed but only offset. It is noted that the calcium is not removed. However, the instant claims as recited do not recite that calcium is removed. This is not found persuasive because as stated above the instant claims incorporate an amount of calcium and since it is unclear how much calcium is present in the instant claims it is the Examiner's position that the Uenoyama et al reference still reads on the instant claims.

Further,

Applicant argues that the Berry et al reference uses a sodium sensitive enzyme and a sodium sensitive ion which binds to sodium ions, the concentration of which is being determined and that the Berry et al reference does not disclose the use of a selective reagent to selectively remove the interferent. It is noted that Berry et al primarily teaches sodium. However, Berry et al also teaches the method may also be used for calcium (abstract) and Berry et al specifically teaches the use of selective binding agents for the binding of interfering ions (col 4, lines 53-55). Further, Berry et al specifically teach that these binding agents are chelating agents such as EDTA or EGTA (which bind to bivalent cations (i.e. calcium)) (col 5) and Berry et al further discloses the function of the binding agent is the selective binding of interfering ions. Berry et al further disclose the advantages of using such selective binding agents (col 3,

lines 45-52). Further, it would have been obvious to one of ordinary skill in the art to present an optimum concentration of chelating agent to optimize the assay.

Applicant also argues that Uenoyama et al. and Berry et al. do not render obvious the trypsin inhibitor assay of the present invention in the wet form and the inclusion of May et al. does not render it obvious in the dry form. As noted above it is the Examiners position that Uenoyama et al. and Berry et al. do render obvious the trypsin inhibitor assay of the present invention in the wet form. As stated by Applicant May et al. is cited for its teaching of a dry test device into which the reagents are incorporated into a test strip. Therefore, as noted in paper number 2, it would have been obvious to one of ordinary skill in the art to impregnate reagents in a dry form into a test device.

Applicant also argues that while the substrate for trypsin may be disclosed by Nanbu et al., Claim 10 depends on claim 1 which has been shown to be novel and unobvious. It is the Examiner's position that claim 1 has not been shown to be novel and unobvious. Therefore, as stated by Applicant the substrate for trypsin is disclosed by Nanbu et al and would have been obvious to one of ordinary skill in the art to incorporate the trypsin substrates of Nanbu et al into the method of Uenoyama et al as modified by Berry et al.

### ***Conclusion***

10. No claims are allowed.
11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

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Okamoto et al (WO/99/49076) disclose a method for assaying urinary trypsin inhibitor.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Gary W. Counts  
Examiner  
Art Unit 1641  
January 29, 2003



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